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| EXAMINER |
|---|
| STEADMAN, DAVID J |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | 14 |

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/937,243 | FROST ET AL. | |
| | Examiner | Art Unit | |
| | David J Steadman | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *58-83 and 85-117* is/are pending in the application.

4a) Of the above claim(s) *70-78,85,86 and 98-104* is/are withdrawn from consideration.

5)☒ Claim(s) *117* is/are allowed.

6)☒ Claim(s) *58-69,79-81,83,87-97 and 105-116* is/are rejected.

7)☒ Claim(s) *82* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Status of the Application*

**[1]** Claims 58-83 and 85-117 are pending in the application.

**[2]** Applicant's cancellation of claim 84, amendment to claims 59-61, 80-82, 106-108, and addition of claim 117 in Paper No. 13, filed June 13, 2003, is acknowledged.

**[3]** Claims 70-78, 85, 86, and 98-104 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

**[4]** Applicant's arguments filed in Paper No. 13 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

**[5]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

### *Unity of Invention*

**[6]** Applicant requests clarification of the examiner's statement regarding the reductive conversion of 1,2,3,4-tetrahydroxybenzene to 1,2,3-trihydroxybenzene (see item 3 of the Office action of Paper No. 11). This statement was not intended to address novelty of the invention of Group I or III. Instead, the statement was made as an explanation for rejoinder of the claims of Groups I and III. The reductive conversion of 1,2,3,4-tetrahydroxybenzene to 1,2,3-trihydroxybenzene is known in the art. Thus, the invention of Group I would not be patentably distinct from the invention of Group III.

### *Claim Objections*

**[7]** Claim 82 is objected to as being dependent upon a rejected base claim, but otherwise appears to be in condition for allowance.

**[8]** Claims 67 and 114 are objected to in the recitation of "the DNA encoding inositol dehydrogenase". While there is no ambiguity as to clarity of the claim, it appears the claims are intended

to be dependent upon claims 66 and 113, respectively and not claims 58 and 105 as written. It is suggested that claims 67 and 114 be amended to be dependent upon claim 66 and 113, respectively.

***Claim Rejections - 35 USC § 112, First Paragraph***

**[9]** The written description rejection of claims 58-69, 79-81, 83, 87-97, and 105-116 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a previous Office action (see item 11 of Paper No. 11). Applicant argues (beginning at the middle of page 10 of Paper No. 13) that a single representative species can suffice to adequately describe an entire genus. Applicant cites the following case law in support of their argument: *In re Marzocchi*, 169 USPQ 367 (CCPA 1971), *Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398 (Fed Cir 1997), and *Utter v. Hiraga*, 6 USPQ2d 1709 (Fed Cir 1988). Applicant argues the Federal Circuit held in *Regents* that an actual example of a single species representing an entire genus was not excluded and, by extension to the instant case, description of a genus of microbes may be achieved if a representative number of species are described. Applicant argues: 1) the examiner provides no reason why a disclosure of an actual representative species is inadequate to show possession, 2) with regard to the first microbe, nucleotide sequences encoding myo-inositol-1-phosphate synthase from various sources were known in the art at the time of the invention and with regard to the second microbe, at least four microbes expressing inositol dehydrogenase activity were known in the art at the time of the invention. Applicant's arguments are not found persuasive. It is the examiner's position that applicant has failed to describe a representative number of species of the claimed genus of microbes. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the

claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. While applicant provides evidence that nucleotide sequences encoding myo-inositol-1-phosphate synthase from various sources and microbes expressing inositol dehydrogenase activity were known in the art at the time of the invention, it is noted that these nucleotide sequences and microbes are naturally occurring. However, according to the specification, the claims are not so limited to those nucleotide sequences encoding myo-inositol-1-phosphate synthase and/or microbes expressing inositol dehydrogenase activity that are naturally occurring and/or were known in the art at the time of the invention. For example, the specification states, "it is envisaged that many types of fungi, bacteria and yeasts will work in the methods of the present invention. Such microorganisms may be developed by, for example, through selection, mutation, and/or genetic transformation processes" (page 7, lines 19-22 of the specification). Thus, based on the teachings of the specification, it is clear that the recited genus of microbes comprising nucleotide sequences encoding myo-inositol-1-phosphate synthase and microbes expressing inositol dehydrogenase are not intended to be limited to those that are naturally occurring and are, in fact, not so limited. Instead, the genus of microbes encompasses species that are *not* naturally occurring and/or were not known at the time of the invention, i.e., mutant and variant microbes. Such mutant and variant microbes encompass species with substantial variation. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". As the claims encompass widely variant species of microbes, the disclosure of those representative species in the specification and the prior art are insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of microbes. Given the lack of description of a representative number of proteins, the

specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

**[10]** The scope of enablement rejection of claims 58-69, 79-81, 83, 87-97, and 105-116 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a previous Office action (see item 12 of Paper No. 11). Applicant argues (beginning at the top of page 13 of Paper No. 11) the examiner has not demonstrated that the claims are not enabled under the standards set forth in *In re Marzocchi*, 169 USPQ 367 (CCPA 1971) and *In re Wands*, 8 USPQ2d 1400 (Fed Cir 1988). Applicant argues the examiner has not met the burden of supporting the assertions with acceptable evidence or reasoning.

Regarding the breadth of the claims (beginning at page 13 of Paper No. 13), applicant argues the examiner provides no support for the statement that the enablement provided by the specification is not commensurate with the scope of the claims. Regarding the first microbe, applicant argues nucleotide sequences encoding myo-inositol-1-phosphate synthase from various sources tools for isolating such sequences by routine experimentation were known in the art at the time of the invention. Regarding the second microbe, applicant argues that nucleic acids encoding inositol dehydrogenase were known in the art at the time of the invention and no more than routine experimentation would be required to isolate microbes expressing a polypeptide having inositol dehydrogenase activity. Regarding acid catalyzed dehydration, applicant argues the examiner provides no reason why this conversion involves undue experimentation or determination of those conditions other than those disclosed would require undue experimentation. Applicant's arguments are not found persuasive. Regarding the broad scope of microbes, as stated above, while applicant provides evidence that nucleotide sequences encoding myo-inositol-1-phosphate synthase from various sources and microbes expressing inositol dehydrogenase activity were known in the art at the time of the invention, it is noted that these nucleotide sequences and microbes are naturally occurring. In the instant case, the claims are so broad as to encompass mutant and variant nucleotide sequences encoding myo-inositol-1-phosphate synthase and/or microbes

expressing inositol dehydrogenase activity as evidenced by the specification, which states, "it is envisaged that many types of fungi, bacteria and yeasts will work in the methods of the present invention. Such microorganisms may be developed by, for example, through selection, mutation, and/or genetic transformation processes" (page 7, lines 19-22 of the specification). Thus, the claims encompass not only those nucleotide sequences and microbes that are naturally occurring, but also nucleotide sequences and microbes that have yet to be isolated including mutants and variants. The specification fails to provide the necessary guidance for making the entire scope of mutant or variant microbes. Neither the specification nor the prior art provides any guidance as to those nucleotides of myo-inositol-1-phosphate synthase and inositol dehydrogenase coding sequences that may be mutated with an expectation of maintaining the desired activity. Furthermore, neither the specification nor the prior art provides any guidance regarding those selection, mutation or genetic transformation processes of microbes recombinantly or endogenously expressing myo-inositol-1-phosphate synthase or inositol dehydrogenase with an expectation of obtaining a desired microbe. Applicant is invited to provide evidence showing that such guidance and/or knowledge was known in the art at the time of the invention. Regarding the broad scope of conditions for acid catalyzed dehydration, the claims are so broad as to encompass any conditions that would result in acid catalyzed dehydration of myo-2-inosose to yield 1,2,3,4-tetrahydroxybenzene. As stated in a previous Office action, the acid catalyzed dehydration conditions as presented in the specification for converting myo-2-inosose to 1,2,3,4-tetrahydroxybenzene (page 10, lines 6-14) are critical for conversion as applicant states that inososes under acidic conditions are dominated by formation of 1,2,3,5-tetrahydroxybenzene. Neither the specification nor the prior art provide any other conditions under which acid catalyzed dehydration of myo-2-inosose to 1,2,3,4-tetrahydroxybenzene will occur. The examiner invites applicant to show that such knowledge was commonly known in the art at the time of the invention. In this case, the enablement provided by the specification is not commensurate with the broad scope of the claims.

Regarding the amount of guidance and working examples (beginning at page 15 of Paper No. 13), applicant argues phosphatases are ubiquitous and other microbes besides *E. coli* JWF1/pAD1.88A

can be used to practice the invention. Applicant further argues the reference of Posternak, used by the examiner in support of the instant rejection, is unsuitable to support a lack of enablement. To the extent applicant's argument addresses the phosphatase that converts myo-inositiol-1-phosphate to myo-inositol, applicant's argument is found persuasive as applicant demonstrates that at least one phosphatase, alkaline phosphatase, is present in a number of microbes and is not specific for a particular substrate. Regarding applicant's argument addressing the conditions for acid catalyzed dehydration, applicant's argument is not found persuasive. It is noted that applicant has also cited the reference of Posternak to demonstrate the disclosed conditions as being critical for conversion of myo-2-inosose to 1,2,3,4-tetrahydroxybenzene as applicant (citing Posternak) states that inososes under acidic conditions are dominated by formation of 1,2,3,5-tetrahydroxybenzene (page 10, lines 6-14). Thus, it is unclear as to how "Posternak is, therefore, inapposite to enablement of the present application". In this case, Posternak is clearly relevant to the instant rejection and application, as demonstrated by applicant's reference to Posternak in showing the recited conditions for acid catalyzed dehydration are critical for making the desired product.

Regarding the unpredictability of the art (beginning at page 17 of Paper No. 13), applicant argues the examiner's statement that different microbes possess distinct metabolic pathways is "mere conjecture" as no evidence has been presented in support of this statement. Applicant's argument is not found persuasive. It is well-known in the art that organisms adapt to their surrounding environment by altering metabolic pathways and/or gene expression to utilize available energy sources and/or adapt to selective pressure. For example, Nelson et al. (*Plant Cell* 10:753-764) teach that in response to increased salinity, levels of myo-inositol-1-phosphate synthase in leaves of ice plant were upregulated, while simultaneously downregulated in roots. Furthermore, Majumder et al. (*Biochem Biophys Acta* 1348:245-256) teach *S. cerevisiae* mutants that lack myo-inositol-1-phosphate synthase activity and further teach repression of myo-inositol-1-phosphate synthase due to inositol in the growth medium. Thus, it is highly unpredictable as to the effects of mutation or environmental stress on the expression of a given nucleic acid in a microbe. As the claims are so broad as to encompass mutant and variant microbes expressing

nucleotide sequences encoding myo-inositol-1-phosphate synthase and/or microbes expressing inositol dehydrogenase activity as evidenced by the specification at page 7, lines 19-22, a skilled artisan would recognize the high degree of unpredictability that mutant and variant microbes developed by selection, mutation, and/or genetic transformation would maintain the characteristics of the parental strain with the ability to produce the desired product.

Regarding the quantity of experimentation necessary, applicant argues (beginning at page 18 of Paper No. 13) applicant argues testing individual microbe species for the appropriate phosphatase activity would not constitute undue experimentation. As stated above, to the extent applicant's argument addresses the undue experimentation to identify those microbes comprising a phosphatase that converts myo-inositiol-1-phosphate to myo-inositol, applicant's argument is found persuasive.

Thus, it is the examiner's position that applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims as determined by an analysis of the Factors of *In re Wands*, 8 USPQ2d 1400 (Fed Cir 1988) as stated in a previous Office action. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

**[11]** In view of applicant's submission of a statement of public availability of the deposited microorganism as an attachment to Paper No. 13, the enablement rejection of claims 61, 63, 65, 84, 90, 92, 94, 108, 110, and 1125 under 35 U.S.C. 112, first paragraph (see item 13 of Paper No. 11), is withdrawn.

***Conclusion***

**[12]** Status of the claims:

- Claims 58-83 and 85-117 are pending.
- Claims 70-78, 85, 86, and 98-104 are withdrawn from consideration.
- Claims 58-69, 79-81, 83, 87-97, and 105-116 are rejected.
- Claim 82 is objected to as being dependent upon a rejected base claim.
- Claim 117 is in condition for allowance.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652

REBECCA E. PROUTY
PRIMARY EXAMINER
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